General

Guideline Title

Management of chronic gout in adults.

Bibliographic Source(s)

University of Texas at Austin, School of Nursing, Family Nurse Practitioner Program. Management of chronic gout in adults. Austin (TX): University of Texas at Austin, School of Nursing; 2012 May. 27 p. [26 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Strength of recommendations (A, B, C, D, I) and quality of evidence (High, Moderate, Low) are defined at the end of the "Major Recommendations" field.

Prophylaxis Against Recurrent Attacks

Non-steroidal Anti-inflammatory Drugs (NSAIDs) and Colchicine

- Naproxen 250 mg orally twice daily (Gonzalez, 2012; Neogi, 2011; Schumacher et al., 2008) (Grade A, High).
- Indomethacin 50 mg orally three times per day (Epocrates Online, 2012) (Grade B, Low).
- Colchicine 0.6 mg orally once or twice daily (Borstad et al., 2004; Hamburger et al., 2011; Neogi, 2011) (Grade A, High).
- Prophylaxis should be considered during initiation and tapering of uric acid lowering therapy (ULT) and should be continued for 3 to 12 months after reaching the serum uric acid target level (Epocrates Online, 2012; Hamburger et al., 2011) (Grade B, Moderate).

First Line Therapy

Pharmacological

- Initiation of ULT is indicated if >2 acute attacks per year, chronic arthropathy, tophaceous deposits, nephrolithiasis, or radiographic changes of gout. Once it is started, lifelong treatment is recommended (Epocrates Online, 2012; Neogi, 2011; Terkeltaub, 2010) (Grade B, Moderate).
- ULT should not be started until at least 2 weeks after resolution of an acute gout attack (Hamburger et al., 2011; Epocrates Online, 2012) (Grade B, Moderate).

- Assess serum uric acid (SUA) level two weeks after an attack has resolved as it may be falsely low or normal during an attack (Hamburger et al., 2011) (Grade B, Moderate).

Allopurinol

Allopurinol 100 mg daily, increasing 100 mg daily every 2 to 4 weeks (maximum of 800 mg daily) until an SUA level <6.0 mg/dl is reached (Hamburger et al., 2011; Gonzalez, 2012) (Grade B, Moderate).

- Results from a randomized controlled trial (RCT) indicated an increase in treatment success from 29% to 78% when doubling the allopurinol dose from 300 mg/day to 600 mg/day (Reinders et al., "A randomised controlled trial," 2009) (Grade A, High).
- Discontinue allopurinol at the first signs of a rash (Gonzalez, 2012; Hamburger et al., 2011) (Grade B, Moderate).
- SUA level monthly until target SUA level <6.0 mg/dl is reached, then retest every 6-12 months (Hamburger et al., 2011) (Grade B, Moderate).

Febuxostat

If allopurinol intolerance, contraindication, lack of efficacy or impaired renal function serum creatinine level >1.5. (Schumacher et al., 2008) (Grade A, High):

- Febuxostat 40 mg daily; may increase after 2 weeks to 80 mg daily to achieve an SUA of <6.0 mg/dl (Gray & Walters-Smith, 2011) (Grade B, Moderate).
- "At all doses studied, febuxostat more effectively lowered and maintained serum urate levels <6.0 mg/dl than did allopurinol (300 or 100 mg) or placebo in subjects with hyperuricemia and gout, including those with mild to moderately impaired renal function" (Schumacher et al., 2008) (Grade A, High).
- Monitor for signs and symptoms of cardiovascular events. In clinical trials, those treated with febuxostat had higher rates of these events than allopurinol, but not statistically significant. Currently, phase III clinical trials are being conducted to evaluate the safety in patients with cardiovascular comorbidities (Gray & Walters-Smith, 2011) (Grade B, Moderate).

Second Line Therapy

Probenecid

- Begin at 250 mg twice daily, may titrate up monthly to a total of 3 g daily in twice daily divided doses to achieve SUA level <6.0 mg/dl (Hamburger et al., 2011) (Grade B, Moderate).
- Results from an RCT indicated a 65% success rate on probenecid 2000 mg/day (Reinders et al., 2009, "Efficacy") (Grade B, Moderate)
- Used with or as an alternative to allopurinol or febuxostat (Hamburger et al., 2011) (Grade B, Moderate).

Third Line Therapy

Pegloticase

- According to Sundy et al. (2011), pegloticase is indicated for "refractory chronic gout and baseline serum uric acid level of 8 mg/dl or greater and at least one of the following: 3 or more self-reported gout flares during the past 18 months; 1 or more tophi; and gouty arthropathy, defined clinically or radiographically as joint damage due to gout. Patients also had contraindication to treatment with allopurinol or failure to normalize SUA despite 3 or more months of treatment with the maximum medically appropriate allopurinol dose" (Grade B, Low).
- It is administered intravenously, 8 mg every 2 or 4 weeks for 6 months (Sundy et al., 2011) (Grade B, Low).
- Pegloticase has a significant risk profile. Candidates should be referred to a health care provider with expertise in the use of pegloticase (Sundy et al., 2011) (Grade B, Low).
- In roughly 3% of patients, conventional oral urate–lowering agents fail to achieve target uric acid levels of less than 6.0 mg/dL. Pegloticase was developed for this group of patients (Brooks, 2011) (Grade C, Low).

Lifestyle Modifications

- Avoidance of purine rich foods (liver, kidneys, shellfish and red meat) (Crittenden & Pillinger, 2011) (Grade B, Moderate)
- Avoidance of beer and liquor (Crittenden & Pillinger, 2011) (Grade B, Moderate)
- Soy beans, vegetable protein sources and cherries (Crittenden & Pillinger, 2011) (Grade B, Moderate)
- Low-fat dairy products, such as yogurt and skim milk reduce uric acid levels (Crittenden & Pillinger, 2011) (Grade B, Moderate).
- Coffee, both caffeinated and decaf, reduces uric acid levels (Crittenden & Pillinger, 2011) (Grade B, Moderate).

- Reducing fructose intake is an important to measure to prevent hyperuricemia (Choi & Curhan, 2008) (Grade B, Moderate).
- Avoidance of aspirin (Grade A, High)
- Increase vitamin C supplementation by an additional 500 mg daily (Grade B, Moderate).
- Weight reduction and lower insulin resistance (Grade A, High) (Zychowicz, Pope, & Graser, 2010)

Definitions:

Strength of Recommendation (Based on U.S. Preventive Services Task Force [USPSTF] Ratings)

A: The USPSTF recommends the service. There is high certainty that the net benefit is substantial.

B: The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.

C: The USPSTF recommends against routinely providing the service. There may be considerations that support providing the service in an individual patient. There is at least moderate certainty that the net benefit is small.

D: The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.

I statement: The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.

Quality of Evidence

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as: • The number, size, or quality of individual studies • Inconsistency of findings across individual studies • Limited generalizability of findings to routine primary care practice • Lack of coherence in the chain of evidence As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: • The limited number or size of studies • Important flaws in study design or methods • Inconsistency of findings across individual studies • Gaps in the chain of evidence • Findings not generalizable to routine primary care practice • Lack of information on important health outcomes More information may allow estimation of effects on health outcomes.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Chronic and recurrent gout

Guideline Category

Management

Prevention

Treatment

Clinical Specialty

Family Practice

Geriatrics

Internal Medicine

Nursing

Nutrition

Rheumatology

Intended Users

Advanced Practice Nurses

Dietitians

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To manage chronic gout and to prevent recurrent disease exacerbations by reducing uric acid levels through pharmacological and lifestyle interventions thereby providing prompt termination of pain and disability

Target Population

Adults with previously diagnosed gout

Interventions and Practices Considered

Treatment/Management

1. Prophylaxis against recurrent attacks

    - Non-steroidal anti-inflammatory drugs (NSAIDs) such as naproxen or indomethacin
    - Colchicine
2. First-line therapy with allopurinol or febuxostat
3. Second-line therapy with probenecid
4. Third-line therapy with pegloticase
5. Lifestyle modifications
    - Low purine diet
    - Increased low-fat dairy foods
    - Avoidance of alcohol ingestion-specifically beer and liquor
    - Regular exercise
    - Increased coffee intake
    - Avoidance of aspirin
    - Increased vitamin C intake
    - Weight reduction and lowered insulin resistance
6. Monitoring of serum uric acid levels and gout symptoms
7. Monitor for signs and symptoms of cardiovascular events

Major Outcomes Considered

- Prevention of recurrent attacks and chronic joint destruction
- Decreased uric acid level (less than 6 mg/dl)

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Searches were conducted via electronic databases including UpToDate, Cochrane Library, Evidence-based Approach, PubMed, CINAHL, and MEDLINE, using key words gout, treatment, uric acid, allopurinol, febuxostat and chronic. The literature search performed was for the past 5 years, 2007-12. However one study from 2004 was included because of its significance.

Number of Source Documents

26

Methods Used to Assess the Quality and Strength of the Evidence

Subjective Review

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as: • The number, size, or quality of individual studies • Inconsistency of findings across individual studies • Limited generalizability of findings to routine primary care practice • Lack of coherence in the chain of evidence As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: • The limited number or size of studies • Important flaws in study design or methods • Inconsistency of findings across individual studies • Gaps in the chain of evidence • Findings not generalizable to routine primary care practice • Lack of information on important health outcomes More information may allow estimation of effects on health outcomes.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Not stated

Rating Scheme for the Strength of the Recommendations

Strength of Recommendation (Based on U.S. Preventive Services Task Force [USPSTF] Ratings)

A: The USPSTF recommends the service. There is high certainty that the net benefit is substantial.

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is moderate to substantial.

C: The USPSTF recommends against routinely providing the service. There may be considerations that support providing the service in an individual patient. There is at least moderate certainty that the net benefit is small.

D: The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.

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Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Not stated

Evidence Supporting the Recommendations

References Supporting the Recommendations

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Type of Evidence Supporting the Recommendations

The type of supporting evidence is specifically stated for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Management of chronic gout symptoms and prevention of recurrence

Potential Harms

Adverse Effects of Medications

- Non-steroidal anti-inflammatory drugs (NSAIDs) are associated with gastrointestinal side effects. Caution should be used in patients with concomitant anticoagulant use and cardiovascular disease.
- Colchicine is associated with nausea, vomiting, and diarrhea.

Contraindications

Contraindications

- *Non-steroidal anti-inflammatory drugs (NSAIDs)* are contraindicated in patients with gastrointestinal (GI) ulcers or bleeding, on anticoagulant therapy and renal insufficiency (creatinine clearance [ClCr] <30 ml/min).
- *Allopurinol* is contraindicated with renal insufficiency and/or renal failure, chronic hepatitis, and allopurinol sensitivity. Thiazide diuretics can inhibit the excretion of allopurinol and potentiate allopurinol toxicity; allopurinol can increase drug levels of theophylline, warfarin, and azathioprine. Metabolism of azathioprine and 6-mercaptopurine is inhibited, leading to serious neutropenia.
- *Febuxostat* is contraindicated in patients concurrently using azathioprine, mercaptopurine, or theophylline. Caution should be encouraged in patients with severe renal insufficiency (ClCr of <30 ml/min) or severe hepatic impairment. Febuxostat is not recommended in children, those being treated for Lesch-Nyhan syndrome, cancer or organ transplants.
- Avoid *colchicine* in patients with severe renal or hepatic impairment because it can lead to bone marrow suppression and neuromyopathy. Interacts with cyclosporine, macrolides, and statins.
- *Uricosuric agents (probenecid)* are contraindicated in patients with urolithiasis, nephrolithiasis and renal insufficiency. Their use is strongly discouraged in patients with history of renal calculi as the uricosuric agents may further promote nephrolithiasis. Their use is not recommended in elderly patients, those on multiple medications (because of multiple drug interactions), or in patients who have trouble complying with multiple daily doses. Probenecid has known interactions with azathioprine, rifampin, salicylates, penicillins, indomethacin, and heparin.
- *Pegloticase* is contraindicated in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency because of the risk for hemolysis and methemoglobinemia. Caution and close monitoring is advised when administering pegloticase to patients with congestive heart failure.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

University of Texas at Austin, School of Nursing, Family Nurse Practitioner Program. Management of chronic gout in adults. Austin (TX): University of Texas at Austin, School of Nursing; 2012 May. 27 p. [26 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 May

Guideline Developer(s)

University of Texas at Austin School of Nursing, Family Nurse Practitioner Program - Academic Institution

Source(s) of Funding

University of Texas at Austin, School of Nursing, Family Nurse Practitioner Program

Guideline Committee

Not stated

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Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: None available.

Print copies: Available from University of Texas at Austin, School of Nursing. 1700 Red River, Austin, Texas, 78701-1499, Attn: Nurse Practitioner Program.

Availability of Companion Documents

None available

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on July 24, 2012. This summary was updated by ECRI Institute on September 18, 2015 following the U.S. Food and Drug Administration advisory on non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs).

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